

I. REMARKS

Claims 1 and 3 to 14 are currently pending. Claims 1 and 3 to 8 are currently under examination.

Regarding the obviousness rejections

1. The '676 patent and Brittberg.

Claims 1, 3, 4, 7 and 8 are rejected under 35 U.S.C. sec. 103(a) as allegedly obvious over U.S. Pat. No. 4,469,676 (the '676 patent) in view of Brittberg et al., New England J. of Med., 331:889-95 (1994). The Office Action argues that it would have been obvious to use the composition taught by Brittberg to treat wrinkles at the site taught by the '676 patent. Applicants respectfully traverse the rejection.

a. The '676 patent teaches away from the invention.

The '676 patent teaches using treating wrinkles by injecting sterile cartilage particles. The '676 patent therefore teaches away from the subject invention in two respects. For this reason alone (regardless of Brittberg), the rejection must be withdrawn.

i. The '676 patent requires particles.

Firstly, the '676 patent requires the use of particles. Indeed, the patent states that a composition of

cartilage particles of less than 40 microns "is not suitable." Column 1, line 65 to column 2, line 2. By contrast, as currently recited in pending claim 1, the subject invention requires cartilage-producing cultured cells "devoid of solid particles" altogether. Thus, the '676 patent teaches away from the subject invention.

For this reason alone, the teaching of the '676 patent could never allow the skilled artisan to practice the subject invention, even in view of Brittberg. It would not have been obvious to take the composition of Brittberg and introduce it at a skin site to treat wrinkles, as taught by the '676 patent, because the '676 patent specifically and clearly teaches to use particles at the skin site to treat wrinkles. In other words, it cannot be obvious to combine a primary reference (the '676 patent) with a secondary reference (Brittberg) when such combination would clearly be teaching away from the primary reference.

**ii. The '676 patent requires sterile cartilage.**

The '676 patent teaches away from the invention in a second respect. As recited in claim 1, the '676 patent requires that the cartilage be sterile. By contrast, the subject invention requires that the cells be cultured, isolated and "cartilage producing." The skilled artisan would therefore not have been motivated to combine the '676 patent with another references, such as Brittberg, resulting in a method that the '676 patent teaches away from in two respects.

**b. The skilled artisan would not have been motivated to apply the composition of Brittberg to a skin site.**

Even if, for the sake of argument, the '676 patent did not teach away from the subject invention (which it does), the rejection must still be withdrawn because it would not have been obvious to apply the composition of Brittberg, which is taught at a site in the knee, at a skin site. In support of this contention, Applicants introduce the declaration of Dr. Abraham Amir (Amir decl.), attached hereto.

Brittberg teaches using chondrocytes to treat deep cartilage defects in the knee. It would not have been obvious to take such a teaching and apply it for use at a skin site for two reasons.

**i. Brittberg does not teach or suggest introducing cartilage producing cells to a non-natural site.**

Firstly, the knee is a natural site for cartilage producing cells. This is why cartilage is naturally found at this site. By contrast, the skin is not a natural site for cartilage producing cells. While the knee has the natural nutritional, fluid and oxygen environment to promote cartilage production from cells, the skin has a different environment. Amir decl., para. 5. Therefore, one would not have been motivated to take the composition of Brittberg and apply it for skin use.

Applicants note that the '676 patent does not cure this defect in Brittberg because that patent teaches

sterile cartilage and not cultured, isolated and cartilage producing cells, as required by the claimed invention. Indeed, no references teaches or suggests a hallmark of the subject invention - introducing cartilage producing cells at a skin site.

**ii. Brittberg does not teach or suggest introducing cartilage producing cells at a site with undefined borders.**

Secondly, applying proliferating cells at a skin site requires great care and control. As stated in the subject application, care should be exercised not to overfill the contour irregularity because the cells being introduced to the site can grow and proliferate. Page 18, lines 1-2.

This kind of care and control is not important at a deep knee site such as the one described by Brittberg, where overgrowth and overproliferation of cartilage are not major concerns because the deep knee site of Brittberg has limited space with solid borders. By contrast, a skin site has undefined borders. Amir decl., para. 6. Therefore, because of concerns of overgrowth and overproliferation, it would not have been obvious to one reading Brittberg to successfully apply that teaching to a skin site.

**c. Long-felt need.**

Lastly, the subject invention address a long-felt need. If indeed Brittberg, which was published a decade ago, and the '676 patent, which issued two decades ago,

could be combined to obviate the subject invention, the subject invention would already have been made.

However, none of the products currently developed include actively proliferating cells, a hallmark of the subject invention. See Chapter 16 of Atlas of Cosmetic Surgery (W.B. Saunders Co. 2002), attached hereto as Exhibit A.

**d. Summary**

In summary, the obviousness rejection must be withdrawn to two reasons. First, the '676 patent teaches away from the invention. Second, because the skilled artisan would not have been motivated take the composition used at a deep knee site, as taught by Brittberg, and apply it at a skin site. In support against obviousness, Applicants' invention addresses a long-felt need. For these reasons, Applicants respectfully request that the rejection of the claims as allegedly obvious be withdrawn.

**2. The '676 patent, Brittberg and Atala.**

Claims 5 and 6 are rejected under 35 U.S.C. sec. 103(a) as allegedly obvious over the '676 patent in view of Brittberg and in further view of Atala et al., J. Urol., 150:745-47 (1993). Applicants respectfully traverse the rejection.

As discussed above, the '676 patent teaches away from the invention. Moreover, as discussed above, because the

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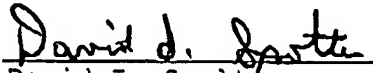
skilled artisan would not have been motivated take a composition used at a deep knee site, as taught by Brittberg, and apply it at a skin site. For these reasons, Applicants respectfully request that this rejection be withdrawn.

## II. CONCLUSION

In light of the Remarks made herein, Applicants respectfully submit that the claims are now in condition for allowance and request a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned attorney.

Respectfully submitted,

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David I. Spolter  
Registration No. 36,933  
Telephone No. (732) 709-5117  
Facsimile No. (518) 452-5579

HESLIN ROTHENBERG FARLEY & MESITI P.C.  
5 Columbia Circle  
Albany, NY 12203